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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/443,986	11/19/1999	DANIEL JOSEPH OMAHONY	99.1064.US	8043

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Marilou E. Watson
Synnestvedt & Lechner LLP
2600 ARAMARK Tower
1101 Market Street
Philadelphia, PA 19107-2950

EXAMINER	
ROBINSON, HOPE A	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 09/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/443,986	OMAHONY, DANIEL JOSEPH	
	Examiner	Art Unit	
	Hope A. Robinson	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-29,35-39,44-88,114,117-136 and 139-144* is/are pending in the application.

4a) Of the above claim(s) *18-29,35-39 and 44-88* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *114,117-136 and 139-144* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

2. Applicant's response to the Office Action mailed January 13, 2005 on June 15, 2005, is acknowledged.

Claim Disposition

3. Claims 1-17, 27, 30-34, 40-43, 89-113, 115-116 and 137-138 have been cancelled. Claims 139-144 have been added. Claims 18-29, 35-39, 44-88, 114, 117-136 and 139-144 are pending. Claims 114, 117-136 and 139-144 are under examination.

Maintained-Specification Objection

4. The specification remains objected to because of the following informalities:

The specification remains objected to because the priority information is not listed on page 1, for example: "This application claims priority to U.S. Provisional Application No. 60/109,038 filed on November 19, 1998. The objection has been maintained as the response filed on June 15, 2005 did not address this issue.

Maintained-Claim Rejections - 35 USC ∋ 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 114, 117-136 and 139-144 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 114 and the dependent claims hereto are directed to a retro-inverted peptide comprising SEQ ID NOS:1-3; said sequences are 15, 16 and 14 amino acids in length, respectively. The claims encompass a genus of peptides, which are highly variable and which are not adequately described; no functional language is recited in the claims nor does the specification demonstrate retention of function for the fragments to demonstrate possession of the genus of the claimed invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and

formulas that fully set forth the claimed invention. See *Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir.1997).*

In addition, claim 126 and its dependent claims are directed to a composition comprising a chimeric protein that comprises the retro-inverted peptide that is bound to an active agent, said active agent being of value in the treatment of a mammalian disease or disorder selected from the group consisting of hypertension, diabetes, osteoporosis, hemophilia, anemia, cancer, migraine and angina pectoris. Claim 126 and its dependents require even less structure by virtue of the language "or binding portions thereof", which is indicative of a large genus of proteins, not adequately described. The specification fails to provide any additional representative species of the claimed genus to show that applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described are representative of the entire genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings, or by disclosure of relevant identifying characteristics, for example, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Further, *Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991)*, states that "applicant must convey with reasonable clarity to those

skilled in the art that, as of the filing date sought, he or she was in *possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of encoded proteins, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. *See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993). See MPEP 2163.*

Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

6. Claims 114, 117-136 and 139-144 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the retro-inverted peptide consisting of the specific sequences (SEQ ID NOS: 1-3), does not reasonably provide enablement for fragments of the claimed peptides or a composition for treatment of all the mammalian disease or disorder encompassed in the claims. The enablement requirement refers to the requirement that the specification describe how to make and

how to use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to:

I. Quantity of Experimentation Necessary:

The claimed invention is directed to a retro-inverted peptide and fragments of the claimed peptide (see for example claims 114 and 117-120). Claim 114 for example, is directed to a peptide that comprises SEQ ID NOS:1-3, which reads on a full-length sequence, however can have fragments added to the N or C terminus and the claim has been amended to remove functional language. In addition, claim 117 for example, is directed to fragments of the claimed peptides with no indication as to a function that is the same as the wild-type or different; or whether there's no biological activity. The art recognizes that the structure-function relationship of a peptide can be dramatically affected by structural changes. For example, claims such as 117-120 recite "wherein the peptide comprises no more than 50 amino acid residues; no more than 40 amino acid residues; no more than 30 amino acid residues and no more than 20 amino acid residues and there is no indication that these fragments will retain the activity or have a different biological activity; no indication of conserved regions or whether the sequence consists of 50 contiguous residues for instance. The claimed peptide consists of SEQ ID NOS: 1-3; said sequences are 15, 16 and 14 amino acids in length, respectively and there is no indication in the claims or the instant specification where in the structure the additions contemplated in claims 117-120 will occur or if the structure can tolerate such

modifications. Moreover, the claims are directed to a composition, comprising a chimeric protein bound to a material comprising an active agent, said chimeric protein comprising the peptide or a binding portion thereof fused to a second protein, in which the active agent is of value in the treatment of a mammalian disease, several of which are recited in the claim (see claim 126, for example). Thus, the claimed composition includes fragments of the claimed peptides. A skilled artisan would have to engage in undue experimentation to be to construct the peptides as claimed and test same for biological activity. Furthermore, there is no indicia as to how to ascribe value to the active agent, which is simply defined as a drug or the laundry listing of agents provided in the claims. The instant specification provides support for the laundry lists of agents, however, no exemplification is provided to enable utilization of the entire listing in the claimed composition. Neither the claims nor the specification provides any showing of the claimed fragments in association with the claimed invention to enable one skilled in the art to be able to practice the full scope of the claimed invention, without undue experimentation.

II. Amount of direction or guidance presented:

The specification does not provide adequate guidance to be able to practice the claimed invention commensurate in scope with the claims. To examine every fragment to determine function/biological activity would require undue experimentation. In addition, there is no indicia as to the binding specificity to the receptors and if the peptide fragments will retain the binding activity. Furthermore, no guidance is provided

as to the claimed diseases or disorders in association with the claimed peptide/fragments and what value is to be placed to obtain a peptide/peptide fragment that results in treatment of the recited diseases/disorders.

III. Presence or absence of working examples:

The working example provided discusses an animal study involving the bioavailability of insulin (see for example page 26, Table 5 of the specification), however, this example does not provide support for the unspecified amount of fragments encompassed by the claims or all the diseases claimed. Therefore, it is difficult to ascertain the nature of the claimed invention from this one record.

IV. Nature of the Invention:

The nature of the invention is a retro-inverted peptide or fragment that specifically binds to gastro-intestinal tract receptor. However, the specification does not provide sufficient guidance/direction to enable the full scope of the claimed invention as the claimed derivative/fragment is not described by size, length or function.

V. State of the prior art and Relative skill of those in the art:

It is disclosed in the specification on page 3 that the applicants have found retro-inverted forms of the GIT targeting agents specific receptor sites *in vivo* and/or promote uptake of active agents and/or enhance active agent delivery across the GIT into the systemic circulation. The claims are directed to fragments of the peptides and no

characteristics or attributes of these have been described. As the prior art is silent on the claimed sequences a high level of skill was required at the time the application was filed.

VI. Predictability or unpredictability of the art:

Since very little is known in the prior art about the nature of the invention, renders the art unpredictable. The claimed invention is directed to fragments and it is highly unpredictable to target sequences when embedded in other sequences. Thus, the specification should then give more details as to how to make and use the invention in order to be enabling.

VII. Breadth of the claims:

The breadth of the claims are very broad and encompass a wide range of diseases and any fragment of the claimed sequences. The specification does not provide support for the broad scope of the claims, which encompass an unspecified amount of fragments and a plurality of agents and diseases/disorders without any association to the claimed composition. The issue in this case is the breath of the claims in light of the predictability of the art as determined by the number of working examples, the skill level artisan and the guidance presented in the instant specification and the prior art of record. This make and test position is inconsistent with the decisions of *In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)* where it is stated that "...scope of claims must bear a reasonable correlation to scope of enablement provided

by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).* Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

7. Claim 135 is rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter, which applicant (s) regard as their invention. Claim 135 is incomplete as the claim depends from cancelled claim 137, thus indefinite. In addition, claim lacks clear antecedent basis as it should depend from claim 134.

Response to Arguments

8. Applicant's remarks made in the amendment filed on June 15, 2005 have been considered. Note that the objection to the specification has been maintained as the response did not address this issue. In addition, the rejections under 35 U.S.C. 112, first paragraph written description and enablement have been maintained. The discussion of the two rejections will be combined as applicant has overlapping arguments. Note also that a new ground of rejection has been instituted under 35 U.S.

C. 112, second paragraph for the reasons stated above based on amendments made to the claim.

On pages 16-17 of the amendment, applicant state that claim 114 has been amended to recite sequences (SEQ ID NOS:1-3), thus defining the structure of the peptide. It is further stated that claims 121 and 126 (have been amended to recite specific diseases) pertaining to compositions for treatment comprising an active agent are fully supported by the specification. Applicant points to pages 7 and 9 of the instant specification (pertaining to the active agents). Additionally, on page 17 it is stated that claim 114 as amended is directed to specific sequences not fragments.

This argument is not persuasive for the reasons of record and set forth above. The instant claims are directed to a retro-inverted peptide comprising the above sequences (claim 114) wherein the peptide can comprise no more than 50 amino acids (claim 117); no more than 40 amino acids (claim 118), no more than 30 amino acids (claim 119); no more than 20 amino acids (claim 120); and a composition comprising the peptide bound to material comprising an active agent being of value in the treatment of the recited diseases in claim 121 and the active agents are listed in claims such as 126.

The claims recite the open language of comprising which indicates that fragments can be added to the sequences in claim 114 on the N and C terminus and claims such as claims 117-120 are directed to fragments of the claimed sequences and there is no recitation of function for the full-length sequences or the fragments. Note that there is no requirement for the 50 or 40 or 20 amino acids recited in the claims to be

contiguous. There is no indication of a conserved region or maintenance of any function with the fragments. Moreover, the peptide is in a composition comprising an active agent that is said to have value in treating diabetes, osteoporosis, angina pectoris, cancer, anemia, hemophilia, hypertension and migraine and the instant specification does not provide any showing of a drug with the claimed peptide in dosage form to treat any of the above diseases. Further, there's no showing that protein exists in altered forms in the diseases listed, for example, an over production or deficiency. In other words, the specification does not disclose that the peptide is expressed in cancer tissues for example, at altered levels or forms. Thus, it is not a target for drug development, toxicology studies, or disease diagnosis. Absent a disclosure of altered levels or forms of a gene in diseased tissue as compared with the corresponding healthy tissue, the gene is not a disease marker or an appropriate target for drug discovery or toxicology testing.

Pages 7 and 9 pointed to by applicant, provides a laundry list of active agents. There is no one to one correlation made between the claimed peptide and the diseases listed. Furthermore, the claims recite the language, "active agent being of value in the treatment" and there is no indication of what value the active agent plays. Thus, in view of the foregoing the claimed invention requires undue experimentation, for a skilled artisan to practice the invention commensurate in scope with the claims and lacks adequate written description pertaining to the invention. Applicant has not demonstrated possession of the genus of peptides encompassed in the claims or demonstrated such in a medicament. Therefore, the rejections have been maintained.

Conclusion

9. No claims are allowable.

10. Applicant's amendment necessitated the new/modified ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr, can be reached at (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson, MS HR
8/24/05
Patent Examiner

KATHLEEN M. KERR, PH.D.
SUPERVISORY PATENT EXAMINER